Simultaneous presentation of multifocal choroiditis and acute zonal occult outer retinopathy in one eye

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CASE

A 20-year-old healthy female patient with moderate myopia who had a bipolar disorder was referred to us by her primary ophthalmologist because of a 3-year history of photopsia and painless visual field loss in her right eye that had accelerated in the past 7 months. She had not been taking any medications except oral contraceptives.

The patient had been referred to a neuro-ophthalmologist 2 months before our visit.

Clinical examination of the right eye revealed a relative afferent pupillary defect and a dense temporal field defect that appeared to respect the vertical meridian, with some involvement of the fovea (figure 1). The retinal pigment epithelium (RPE) changes in the temporal fundus (figure 1) were interpreted as a demarcation line from an antecedent retinal detachment. At that time, the patient was found as having a right optic neuropathy. Subsequently, a magnetic resonance imaging of the brain was performed, which yielded an unremarkable result. The finding of an extensive inflammatory, infectious and haematologic laboratory workup was negative.

Upon examination in our office, the patient's best corrected visual acuity was 20/30 in the right eye and 20/20 in the left eye. Intraocular pressure was 16 mm Hg bilaterally. A mild cellular reaction was seen in the anterior vitreous of the right eye. The fundus of the right eye revealed peripapillary atrophy and a focal area of hyperpigmentation located inferotemporally to the optic nerve. There were multiple round greyish yellow punched-out lesions with variable pigmentation arranged in a curvilinear streak in the temporal periphery of the retina (figure 1). The fundus of the left eye was normal except for a small temporal myopic conus and a subtle non-specific RPE disturbance just inferior to fixation.

Fundus autofluorescence (AF) photography of the right eye demonstrated hypoautofluorescence surrounding the optic nerve that was more intense temporally due to presumed RPE damage (figure 1). The temporal curvilinear streak appeared hypoautofluorescent secondary to RPE alterations. Fluorescein angiography (FA) of the right eye demonstrated staining of the temporal chorioretinal spots with some subtle window defects surrounding the optic nerve (figure 1).

QUESTIONS

1. What is the differential diagnosis based upon the biomicroscopic findings, the visual field, the AF photography and the FA?
2. What other test(s) would help clarify the diagnosis?

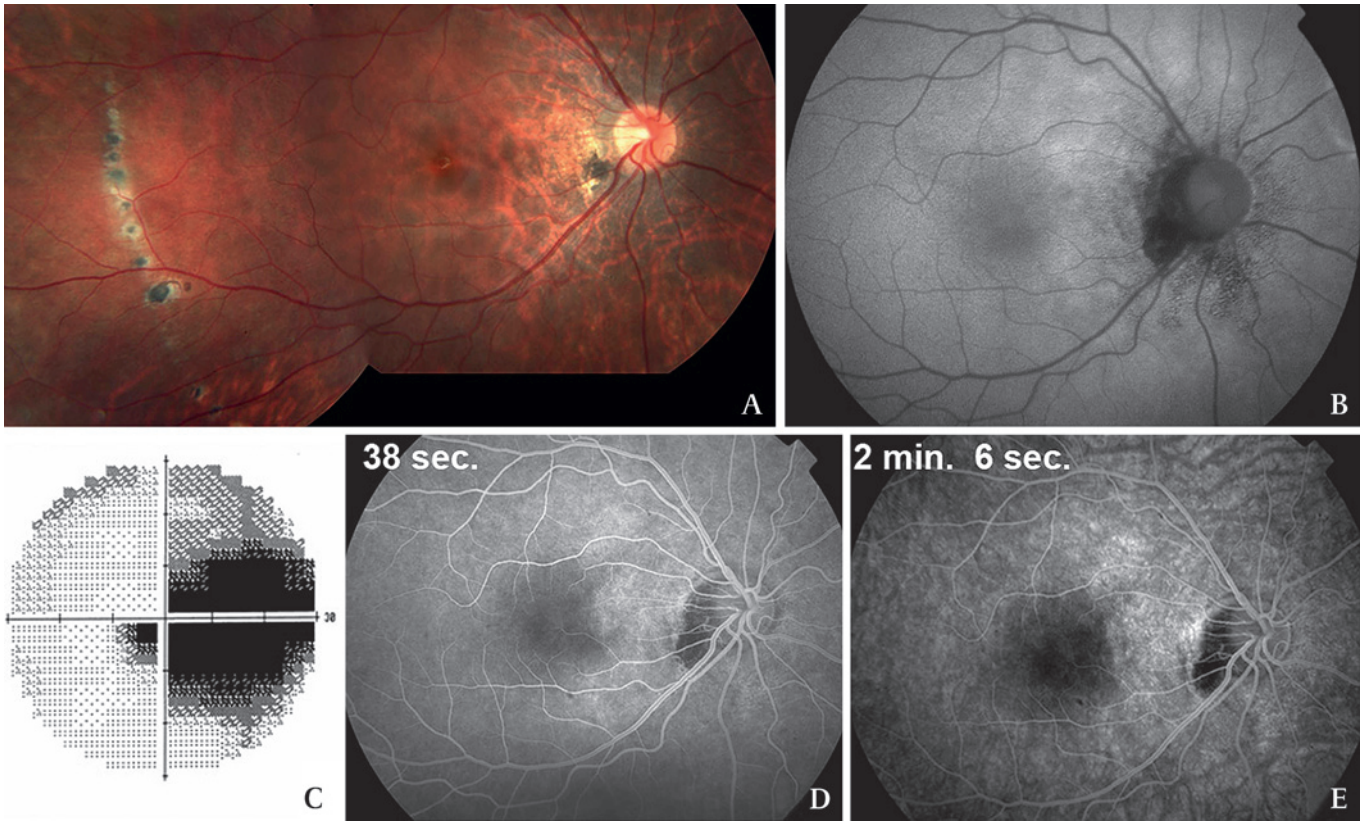

Figure 1 (A) Composite photograph of the right fundus showing both punched-out chorioretinal lesions in the temporal periphery forming a curvilinear streak and peripapillary pigmentary alterations. (B) AF photograph of the right eye revealing RPE abnormalities surrounding the optic nerve. (C) The visual field of the right eye demonstrates a moderately dense temporal scotoma that respects the vertical meridian except in the parafoveal area where the scotoma extends slightly inferior to fixation. (D/E) FA of the right eye demonstrating staining of the temporal chorioretinal spots with some very subtle window defects surrounding the optic nerve.

3. How should this patient be treated?
See page 297 for answers

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ANSWERS

From questions on page 288

1. What is the differential diagnosis based upon the biomicroscopic findings, the visual field, the autofluorescence photography and the fluorescein angiography (FA)?
   This patient exhibited two of the signs in the clinical triad of the presumed ocular histoplasmosis syndrome (POHS), which includes peripapillary atrophy, disseminated punched-out atrophic spots and choroidal neovascularisation. Fountain and Schlaegel[1] noted that peripheral curvilinear streaks composed of chorioretinal scars can be a fourth sign of POHS (figure 1). The convexity of these curvilinear streaks is typically orientated towards the optic nerve unlike the pigmented demarcation line in rhegmatogenous retinal detachment that is usually oriented towards the ora serrata. Thus, many of the ocular findings of POHS are similar, if not identical, to multifocal choroiditis with panuveitis (MCP). The presence of intraocular inflammation in MCP is the critical feature distinguishing it from POHS,[2 3] but this finding may be episodic.

   Enlarged blind spots or visual field defects correlating to the fundus lesions are seen in MCP. This patient's large right temporal field defect is out of proportion to her funduscopic findings. Gass first described an idiopathic condition where patients, usually young women, developed photopsia and acute progressive visual field loss in one or both eyes due to damage of broad zones of the outer retina. He termed this pattern *acute zonal occult outer retinopathy* (AZOOR).[4] The hallmark of this disease is that the visual field defect is unexplained by the fundus findings. Given our patient's sex, age, clinical presentation and relatively normal appearing fundus, the diagnosis is most likely MCP and AZOOR.[4]
2. What other test(s) would help clarify the diagnosis?
   Electrophysiological testing can be helpful for the early diagnosis of AZOOR. The electroretinogram (ERG) typically shows a cone system with 30 Hz flicker delay, indicative of photoreceptor damage. A decreased light rise, indicative of retinal pigment epithelium (RPE) compromise, is seen on electro-oculogram.[5] The severity of ERG abnormalities is variable and generally correlate to the degree of visual field loss,[4] but normal ERG findings have also been reported.

   Our patient underwent Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany), which demonstrated defects in the junction between the inner (IS) and outer segments (OS) of the photoreceptors (the IS/OS boundary) that encroached close to the fovea and corresponded precisely with the visual field defects (figure 2).[7] Given this clear evidence of photoreceptor damage, we did not feel that an ERG was necessary to make the diagnosis in our patient.
3. How should this patient be treated?
   In limited studies, diseases of the AZOOR complex have responded to immunosuppressive drugs. However, since this treatment can take up to 8 weeks to be effective, we elected to treat her initially with a subtenon injection of triamcinolone acetonide in the affected eye in an attempt to more rapidly prevent further vision loss.[4 7 8] We chose not to give oral corticosteroids to avoid systemic and neuropsychiatric adverse effects, especially given her unilateral presentation and the history of bipolar disorder. She was referred to a rheumatologist who initiated mycophenolate mofetil therapy.

DISCUSSION

This case demonstrates the importance of considering retinal disease in the differential diagnosis of acute visual field loss with minimal funduscopic changes, particularly when associated with symptoms of photopsia. A recent report of a 17-month delay in the diagnosis of AZOOR demonstrates the lack of awareness of AZOOR in the current medical community.[9]

AZOOR was first described by Gass, who subdivided it into two groups:[10 11] AZOOR type 1 (occult) with primary retinal receptor involvement and no funduscopic or FA changes corresponding to the visual field loss and AZOOR type 2 (overt) with combined photoreceptor and RPE involvement showing more pronounced fundus and FA changes. Our patient fits more closely in the first category currently. In their long-term follow-up study, Gass *et al* reported that at the onset of AZOOR, the clinical examination result was either normal or revealed changes unrelated to AZOOR in 91% of the affected eyes. On final examination (median follow-up of 96 months), only 52% had normal fundi.[4] The fundus picture of the late stages of AZOOR may mimic that of either typical or segmental forms of retinitis pigmentosa.

AZOOR belongs to the AZOOR complex, which also includes multiple evanescent white dot syndrome and MCP. Common to all of these entities are a female predominance, photopsia, a blind spot enlargement and ERG abnormalities. Gass[11 12] proposed that AZOOR may be pathologically and aetiologically related to multiple evanescent white dot syndrome, acute idiopathic blind spot enlargement syndrome, acute macular neuroretinopathy and MCP. Neither the trigger mechanism nor the pathogenesis is known for any of these diseases. A higher prevalence of autoimmune disease in patients with AZOOR has been reported, but this does not necessarily indicate an

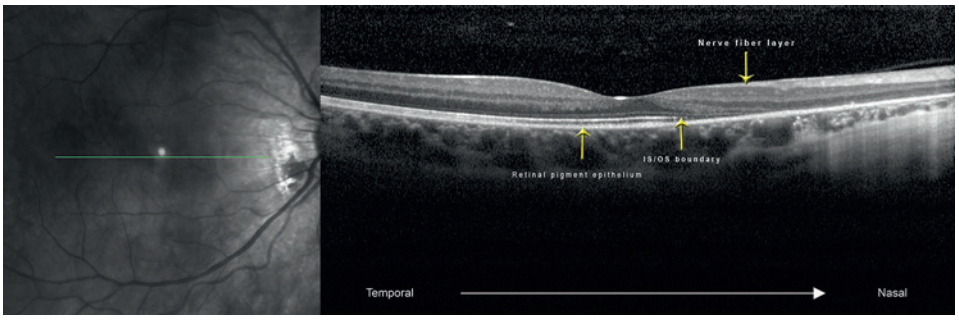

Figure 2 Spectral domain OCT demonstrating photoreceptor loss beginning just nasal to the foveal pit and extending to the optic nerve. The loss of photoreceptors is indicated by the absence of the IS/OS boundary (arrow) representing the junction between the IS and OS of the photoreceptors.[6] In our patient, the IS/OS defects correlate precisely with the visual field abnormalities. Despite the loss of overlying photoreceptors, the RPE (arrow) in the affected areas appears normal.

autoimmune basis for the loss of vision. Our patient's serologic tests and inflammatory markers were negative, and she did not exhibit other features suggestive of a connective tissue or an autoimmune disease. Immunological reactions to previous viral infections coupled with a genetic predisposition seem to be a common denominator.

Transitions between the individual diseases have been described.[12 13] To our knowledge, there have been no other cases reporting the simultaneous presentation of MCP and AZOOR in the same eye.

To differentiate AZOOR from retrobulbar neuritis and other lesions involving the posterior visual pathways, an ERG should be obtained.[4] Jacobson *et al*[14] reported the electrophysiological findings in 24 patients with diagnoses of the AZOOR complex. Their results were in agreement with previous reports suggesting that patients with AZOOR showed a pattern of visual dysfunction that originated in the photoreceptor level. Francis *et al*[5] reported on 28 AZOOR patients and found an electrophysiological pattern consistent with dysfunction both at the photoreceptor/RPE complex and at the inner retinal levels, namely, a delayed 30 Hz flicker ERG and a reduction in the electro-oculogram light rise. These electrophysiological findings may be helpful not only to establish the correct diagnosis but also to monitor progression of disease or results of treatment.

In contrast to electrophysiological testing, high-resolution spectral domain optical coherence tomography (OCT) can directly and unequivocally reveal photoreceptor damage (loss of IS/OS boundary), which correlate to the blind spot enlargement and other visual field defects. Recently, we demonstrated this correlation and also reported restoration of the IS/OS boundary in some AZOOR complex patients with improvement in visual field. Permanent loss of the IS/OS boundary was seen in patients with persistent large visual field defects.[6] The IS/OS boundary defects in our patient coincided precisely with her visual field changes, supporting that the aetiology of her visual defect was retinal as opposed to neurological (figure 2B).

In limited studies, AZOOR and MCP have responded to immunosuppressive drugs in addition to local or oral corticosteroid therapy.[6 15] Both electrophysiological and spectral domain OCT testings are helpful to objectively plot the course of disease. However, whether immunosuppression can meaningfully alter the natural course of disease needs further study.

Final diagnosis

This is a case of multifocal choroiditis and AZOOR presenting simultaneously in the same eye.

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